REMARKS/ARGUMENTS

Status of the claims

Claims 45-57, 60-62, 65-69 and 83 were previously pending. Claim 45 is amended.

Claims 45-57, 60-62, 65-69 and 83 stand rejected as allegedly lacking enablement pursuant to 35 U.S.C. §112, first paragraph.

Response to the rejection of claims 45-57, 60-62, 65-69 and 83 for an alleged lack of enablement.

The enablement rejection is based upon two separate contentions. The first contention is that methods of making the claimed compounds are not enabled. The second contention concerns the nexus between KCNQ2 inhibition and the treatment of anxiety. Applicants address each in turn.

A. Enablement of the synthesis of the compounds of the pending claims.

This aspect of the rejection stands on two basic premises. It is first alleged that the specification lacks adequate guidance and exemplification as to how to make the compounds set forth in the claims. Applicants respectfully rebut this assertion.

The instant application does teach how to make the compound subject matter of the claims. The application incorporates by reference in the first sentence of the specification the disclosure of priority application of U.S. Patent Application Serial No. 60/147221 (enclosed) (also, a priority application of U.S. Patent No. 6,495,550 which is a subject of the maintained rejection for obviousness-type double patenting). The '221 provisional application teaches methods suitable for making the subject compounds in Ex. 2 at p. 21.

The instant application also discloses U.S. Patent Application Serial No. 09/632,576 (now, U.S. Patent No. 6,372,767, enclosed, which also shares priority benefit of the '221 provisional application) and incorporates its disclosure by reference in the first paragraph of the instant specification. Starting with nitro pyridines, nicotinic acids, or halopyridine in Example 1 on col. 17. The '576 patent further describes how to prepare benzanilides from acid

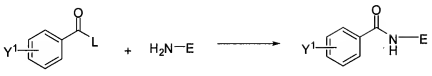
chlorides starting in Ex. 2 on col. 19. Ex. 1 to 8 of the '576 patent discloses and exemplifies a number of synthetic schemes which are also exemplified in making many compounds set forth in the present claims. Accordingly, the Applicants submit that methods of making compounds according to the claims are well supported by the specification as filed.

Applicants further note that, pursuant to 37 CFR §1.57 (c) even essential subject matter if from a U.S. patent application may be incorporated into a patent application by reference. Accordingly, such incorporation by reference of the above subject matter into the instant application is no bar to the enablement of the compound subject matter of the claims.

The second premise relates to alleged deficiencies in knowledge available to persons of ordinary skill in the art to synthesize or obtain compounds set forth in the claims. This premise is wrong. Applicants submit that N-pyridyl benzamide compounds are well-known in the art or can be readily purchased or prepared by a person of skill in the art.

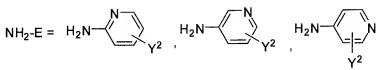
Indeed, a large number of N-pyridyl benzamide compounds or amino pyridines with various substituents are commercially available from suppliers. The ChemExper web directory which lists compounds which are commercially available from a variety of sources was searched to identify compounds containing N-pyridyl benzamide as substructure. o, m, and p forms of the N-pyridyl rings were searched. The home page of the ChemExper directory, which provides its address, and the first 20 compounds listed for each of the separate search results for the o-, m-, and p-pyridyl substructures are presented in Exhibit A.

Furthermore, N-pyridyl benzaamides can be readily prepared according to methods already known in the art, including the synthetic scheme:



a1: L= Cl
a2: OH

c



b1 **b2** **b3**

In the above scheme, benzoic acid chloride (**a1**) is reacted with substituted or unsubstituted 2-aminopyridine (**b1**), substituted or unsubstituted 3-aminopyridine (**b2**), substituted or unsubstituted 4-aminopyridine (**b3**) in the presence of a base, such as triethylamine or NaOH to form the benzamide product (**c**) (see, Webb, *Organic Syntheses,* Coll. Vol. 1, p.82 (1941); Lazier, et al. *Organic Syntheses,*I: 99 (1941); enclosed with Supplemental IDS). Alternatively, N-pyridyl benzamide can be conveniently prepared by reacting commercially available or known benzoic acid **a2** is reacted with substituted or unsubstituted 2-aminopyridine (**b1**), substituted or unsubstituted 3-aminopyridine (**b2**), substituted or unsubstituted 4-aminopyridine in the presence of dicyclohexylcarbodiimide (DCC) as shown in the reaction scheme above (see, Klausner, et al. *Synthesis* 1972, 453-463; and Sheehan *J. Am. Chem. Soc.* 1955, 77, 1067; enclosed with Supplemental IDS).

Accordingly, the Applicants respectfully request that the above grounds of rejection be reconsidered and withdrawn.

B. Enablement of the anxiolysis

The enablement rejection challenges the nexus between the ability of the subject compounds to modulate the KCNQ channels as recited in the claims and their efficacy in treating anxiety. The Applicants' disclosure identified their compounds as anxiolytics based upon their KCNQ channel modulating abilities. The Applicants further confirmed that identification - and demonstrated the existence of the nexus - by testing one of the active compounds for anxiolytic

activity *in vivo*. However, in the spirit of expediting prosecution and without acquiescing on the merits, the Applicants have amended the claims to remove the recital at issue and respectfully request that the above grounds for rejection be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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Attachments
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